REMARKS

I. Status of the Application

Claims 1-51 are presently pending in the application. Claims 14-25 and 27-51 have been withdrawn from consideration. Claims 1, 2, 7-13 and 26 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Claims 1-13 and 26 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Claims 1-13 and 26 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. Claims 1-3, 5-13 and 26 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Walker et al., WO 2002/018575.

Applicants have amended the claims under consideration to more clearly define and distinctly characterize Applicants' novel invention. Specifically, Applicants have amended claims 1 and 2 to clarify that Tome-1 refers to trigger of mitotic entry 1 and that SCF complex refers to Skp-Cullin-F-box protein complex. Claim 2 was further amended to remove the language "which encodes the polypeptide." Claim 3 was amended to replace the language "encodes a nucleotide sequence having" with "has." Claim 5 was amended to recite "wherein the isolated nucleic acid molecule encodes a polypeptide having one or more Tome-1 activities," support for which can be found at least at claim 1. Claim 6 was amended to recite "wherein the polypeptide has one or more Tome-1 activities," support for which can be found at least at claim 1.

The amendments presented herein contain no new matter. Applicants respectfully request entry and consideration of the foregoing amendments, which are intended to place the case in condition for allowance.

II. Objections

At page 3 of the instant Office Action, the specification is objected to because the title contains the word "novel." In response, Applicants have amended the title to remove the word novel. Accordingly, Applicants request that this objection be withdrawn.

At page 4 of the instant Office Action, claims 1-3 are objected to for reciting "Tome-1," "SCF" or "wee1." The Office Action states that the recitation of these terms should be in parentheses and follow the phrase it abbreviates when used for the first time. With respect to "Tome-1" and "SCF," Applicants respectfully submit that claims 1 and 2 have been amended in the manner suggested by the Office Action. Accordingly, Applicants request that these objections be withdrawn. With respect to "wee1," Applicants respectfully submit that this term is a noun, referring to a specific nuclear protein, and is not an abbreviation for a phrase. Indeed, the National Center for Biotechnology Information (NCBI) lists the term wee1 as the official symbol for this protein, and does not provide a phrase that the term wee1 would represent (see Attachment A). Accordingly, Applicants respectfully submit that this objection is improper and ask that it be withdrawn.

III. Claims 1, 2, 7-13 and 26 Are Definite

At page 4 of the instant Office Action, claims 1, 2, 7-13 and 26 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse this rejection.

The second paragraph of 35 U.S.C. § 112 states that:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter

which the applicant regards as his invention.

It is well settled that a claim must "reasonably apprise those skilled in the art both of the utilization and scope of the invention." *Georgia-Pacific Corp. v. United States Plywood Corp.*, 258 F.2d 124, 134-38, 118 U.S.P.Q. 122, 130 (2d Cir. 1958), *cert. denied*, 358 U.S. 884 (1958). Claims 1, 2, 7-13 and 26 meet this standard.

The Office Action asserts that it is not clear with respect to what Applicants intend as being encompassed by Tome-1 and that it is not clear what is encompassed by the "activities" or "activity" of Tome-1 or an SCF complex component. Claim 1 and claims depending therefrom are directed in part to a polypeptide having one or more "Tome-1 activities," not simply Tome-1. Applicants respectfully submit that, based on the teachings of Applicants' specification, one of skill in the art would readily understand what is meant by the term "Tome-1 activities." Applicants teach that Tome-1 activities are: (1) modulating ubiquitinylation of wee1; (2) modulating degradation of wee1 (3) modulating SCF complex components (e.g., Skp-1, Cul-1 and the like); (4) modulating entry of a cell into the cell cycle; (5) modulating progression of a cell through the cell cycle; (6) modulating release of a cell from the cell cycle; (7) modulating cell growth; (8) modulating cellular proliferation; (9) modulating tumorigenesis; and (10) modulating mitogenesis (page 17, lines 7-12). Accordingly, the term "Tome-1 activities" is definite. Therefore, Applicants request that this rejection be reconsidered and withdrawn.

The Office Action states that, with respect to the limitation "the polypeptide" in claim 2, there is insufficient antecedent basis for this limitation in the claim because the subject matter of claim 1 is drawn to an isolated nucleic acid molecule, and not to a polypeptide. Applicants respectfully traverse this rejection as there is proper antecedent basis for the limitation "the polypeptide." However, in the interests of expediting prosecution, Applicants have amended

claim 2 to remove the language "which encodes the polypeptide," thus rendering this rejection moot.

The Office Action states that it is not clear with respect to what Applicants intend as being encompassed by wee1. Applicants respectfully submit that claim 2 recites "wee1 ubiquitinylation" and "wee1 degradation," not simply wee1. As discussed above, Applicants submit that wee1 is an art-recognized protein (See Attachment A) and that protein ubiquitinylation and protein degradation are biochemical processes that are well-known to those of skill in the art (See Attachment B). Furthermore, Applicants' specification teaches one of skill in the art how to detect wee1 degradation and ubiquitination (page 67, Example V and page 70, Example VI, respectively). Accordingly, one of skill in the art would readily appreciate what is meant by the recitation of "wee1 ubiquitinylation" and "wee1 degradation." Therefore, Applicants request that this rejection be reconsidered and withdrawn.

The Office Action states that it is not clear with respect to what Applicants intend as being encompassed by an SCF complex component. The Office Action asserts that it is not clear what is encompassed by the "activities" or "activity" of an SCF complex component. Claim 2 recites "an SCF complex component activity," not simply an SCF complex component. Applicants teach that SCF components are Skp-1, Cul-1, Rbx and the F box substrate receptor protein (specification, page 2, lines 20-21), and it is well-known in the art that the SCF complex consists of these four protein components (See Attachment C). Applicants teach that SCF is a ubiquitin ligase and is one of two of the best-studied E3 ligases active during the cell cycle (specification, page 2, lines 20-22 and page 3, lines 13-14). Accordingly, one SCF complex component activity is an E3 ligase activity. E3 ligases target proteins for proteasomal degradation, and their activities are well-known in the art (See Attachment D). Further,

Applicants teach that the SCF complex can degrade certain substrates such as wee1 and β-catenin (specification, page 3, lines 19-21 and page 68, lines 14-15). Accordingly, one of skill in the art would readily understand what is meant by the term "an SCF complex component activity." Therefore, Applicants request that this rejection be reconsidered and withdrawn.

The Office Action states that claim 3 recites the phrase "the nucleic acid molecule encodes a nucleotide sequence," which is unclear. Without acquiescing to this rejection, Applicants submit that claim 3 has been amended to replace the language "encodes a nucleotide sequence having" with "has," thus obviating this rejection.

Accordingly, Applicants respectfully submit that the pending claims are definite. Therefore, Applicants request that the rejection of claims 1, 2, 7-13 and 26 under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

IV. The Specification Provides Adequate Written Description for Claims 1-13 and 26

At page 6 of the instant Office Action, claims 1-13 and 26 stand rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement for containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Office Action asserts that to satisfy the written description aspect of 35 U.S.C. § 112, first paragraph, for a claimed genus of compositions or methods, it must be clear that: (1) the identifying characteristics of the claimed compositions or methods have been disclosed, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation

between function and structure, or a combination of these; and (2) a representative number of species within the genus must be disclosed.

The first paragraph of 35 U.S.C. § 112 requires that the specification provide a written description of the claimed invention:

> [t]he specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The purpose of the written description requirement is to ensure that the specification conveys to those skilled in the art that the applicants possessed the claimed subject matter as of the filing date sought. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 U.S.P.Q.2d (BNA) 1111, 1117 (Fed. Cir. 1991). With respect to polypeptides, the U.S. Patent and Trademark Office's Written Description Guidelines state:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by . . . disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by ***functional characteristics*** coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus . . . .

66 Fed. Reg. 1099, 1106 (January 5, 2001), internal reference omitted, approved in *Enzo Biochem, Inc. v. Gen-Probe Incorporated*, 296 F.3d 1316, 1325, 63 U.S.P.Q.2d (BNA) 1609, 1613 (Fed. Cir. 2002), emphasis added.

Description of a representative number of species does ***not*** require the description to be of such specificity that it would provide individual support for each species that the genus embraces (MPEP 2163 II (A)(3)(a)(ii)). *Id.* What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. *Id.*

Applicants respectfully submit that the instant specification more than adequately describes the claimed methods with reasonable clarity to one of skill in the art. Applicants teach a combination of identifying characteristics sufficient to show that Applicants were in possession of the claimed genus. Specifically, Applicants teach Tome-1 nucleotide sequences and the corresponding Tome-1 polypeptides, which have a specific sequence identity and the ***functional characteristic*** of having one or more Tome-1 activities.

Applicants submit that the cell cycle field is a well-established discipline that includes highly trained Ph.D. level scientists. Since the skill and knowledge in the art of the cell cycle field is high, what constitutes a representative number of species to provide adequate written description for a claim directed to a genus should be the inverse of such a high level, i.e., only a few species should suffice. Applicants provide ***several examples*** of species that the genus embraces, i.e., human, mouse and *Xenopus* Tome-1 polynucleotides and their corresponding polypeptides which have one or more Tome-1 activities (specification, page 13, lines 1-7). Applicants provide a working example for identifying Tome-1 polypeptides and cDNAs, and for assaying Tome-1 degradation during the cell cycle (Examples I and II).

Applicants teach specific Tome-1 activities: modulating ubiquitinylation of wee1; modulating degradation of wee1; modulating SCF complex components (e.g., Skp-1, Cul-1 and the like); modulating entry of a cell into the cell cycle; modulating progression of a cell through the cell cycle; modulating release of a cell from the cell cycle; modulating cell growth; modulating cellular proliferation; modulating tumorigenesis; and modulating mitogenesis (page 17, lines 7-12). Applicants provide working examples for determining a variety of Tome-1 activities. For instance, Applicants teach methods assaying ubiquitinylation of wee1 (Example VI); methods for assaying wee1 degradation (Example V); methods for detecting Tome-1

interactions with Skp-1 and Cul-1 (Example III); methods for determining modulation of mitotic entry (Examples IV and V); and methods for modulating progression a cell through the cell cycle (Example VII). Methods for determining other Tome-1 activities, such as assaying cell growth, cellular proliferation, tumorigenesis, mitogenesis and the like were well-known in the art at the time of filing.

The specification must be considered as a whole when determining whether the written description requirement is met. *In re Wright*, 866 F.2d 422, 425, 9 U.S.P.Q.2d (BNA) 1649, 1651 (Fed. Cir. 1989). The knowledge of one skilled in the art also must be considered, because the specification must "indicate[s] to persons skilled in the art that as of the [filing] date the applicant had invented what is now claimed." *All Dental Prodx LLC v. Advantage Dental Products Inc.*, 309 F.3d 774, 779, 64 U.S.P.Q.2d (BNA) 1945, 1948 (Fed. Cir. 2002). When read as a whole, taking into account the knowledge of persons skilled in the art at the filing date of the instant application, this specification indicates to those skilled in the art that Applicants had possession of the claimed subject matter at the time of filing. Accordingly, the Examiner is respectfully requested to reconsider and withdraw this rejection of claims 1-13 and 26 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

V. Claims 1-13 and 26 Are Enabled

At page 8 of the instant Office Action, claims 1-13 and 26 stand rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the enablement requirement because the specification, while enabling for an isolated nucleic acid molecules comprising a nucleotide sequence consisting of SE ID NO:5, does not reasonably provide enablement for any isolated nucleic acid molecule which encodes any polypeptide comprising any amino acid sequence

having at least about 60% sequence homology to an amino acid sequence consisting of SEQ ID NO:2, wherein the polypeptide has one or more Tome-1 activities. The Office Action concludes that the specification does not enable any person skilled in the art to which it pertains, or to which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

35 U.S.C. §112, first paragraph requires that the specification must enable a person skilled in the art to make and use the claimed invention. However, a specification need not, and should not, disclose what is well known in the art. The invention that one skilled in the art must be enabled to make and use is that defined by the claims of the particular application. The issue of adequate enablement depends on whether one skilled in the art could practice the claimed invention without undue experimentation. Enablement is not precluded by the necessity of some experimentation such as routine screening, even if it is ***extensive routine screening***. Also, the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation (MPEP 2164.01) if the level of skill in the art is high or if all of the methods needed to practice the claimed invention are well known. *In re Wands*, 8 U.S.P.Q. 2d 1400, 1406 (Fed. Cir. 1988).

> The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art. (Citations omitted). The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *In re Wands*, 8 U.S.P.Q. 2d at 1404.

The Office Action contends that the specification does not support the broad scope of the claims which encompass any nucleic acid molecule which encodes a polypeptide comprising any amino acid sequence having at least about 60% sequence homology to an amino acid sequence

consisting of SEQ ID NO:2, wherein the polypeptide has one or more Tome-1 activities because the specification does not establish: (A) regions of the nucleic acid molecule which may be modified without affecting the desired activity of the encoded protein; (B) the general tolerance of said nucleic acid molecules to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleic acid molecules with an expectation of obtaining the desired biological function of the encoded protein; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Applicants need not claim specific positions in the protein which are tolerant to change, or the nature and extent of changes that can be made in specific positions to enable the claimed invention, as one of skill in the art would easily recognize the claimed nucleic acid sequences encoding the claimed polypeptides having both the claimed sequence identity and the claimed functional characteristic of one or more Tome-1 activities. Determining whether the nucleic acid sequence encodes a polypeptide having the claimed sequence identity and has one or more Tome-1 activities would involve only ***routine screening***. The pending claims recite amino acid or nucleic acid sequences having a specific amino acid sequence identity (i.e., comprising at least 60% or at least 85% sequence homology to a specific sequence identifier (e.g., SEQ ID NO:2, SEQ ID NO:5 or the like)). As discussed above, the instant specification teaches the nucleic acid sequences and amino acid sequences of mouse, human and *Xenopus* Tome-1, and methods of identifying Tome-1 polypeptides and cDNA. One of skill in the art would readily understand whether an amino acid or nucleic acid sequence has the claimed sequence homology by comparing the sequence to the referenced sequence identifier (e.g., SEQ ID NO:2, SEQ ID NO:5 or the like). Applicants provide working examples for preparing Tome-1 antibodies, for

assaying Tome-1 degradation during the cell cycle, and for synchronizing cells for use in cell cycle assays (Example VIII). The instant specification further teaches specific Tome-1 activities and, as discussed above, provides working examples for assaying a variety of Tome-1 activities. Accordingly, based on these teachings, one of skill in the art could easily make and use the claimed amino acid or nucleic acid sequences and the claimed polypeptides having one or more Tome-1 activities.

For at least these reasons, Applicants' specification, coupled with the level of skill in the art, enables a person of skill in the art to make and/or use the claimed invention. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection of claims 1-13 and 26 under 35 U.S.C. § 112, first paragraph.

VI. Claims 1-3, 5-13 and 26 Are Novel Over Walker et al.

At page 11 of the instant Office Action, claims 1-3, 5-13 and 26 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Walker et al., WO 2002/018575. Applicants respectfully traverse this rejection. Applicants respectfully submit that for a reference to anticipate a claim, the reference must teach each and every element of the claim.

The Office Action asserts that Walker et al. teaches an isolated nucleic acid molecule (SEQ ID NO:3) which has 97% sequence homology to Applicants' SEQ ID NO:5, wherein the SEQ ID NO:3 of Walker et al. encodes an amino acid sequence having at least 60% sequence homology to Applicants' SEQ ID NO:2, and wherein the SEQ ID NO:3 of Walker et al. has one or more Tome-activities. The Office Action further asserts that Walker et al. teach that CDC23, which is a protein encoded by SEQ ID NO:3 of Walker et al. is a component of anaphase-promoting complex that regulates mitosis by catalyzing the formation of cyclin B-ubiquitin

conjugates, targeting cyclinB for degradation, thereby anticipating "Tome-1" because it is also a protein that has a destruction box, F box, a KEN sequence or an activity that modulates mitotic entry. Applicants disagree.

First of all, the Office Action provides ***no evidence***, such as a sequence alignment, that SEQ ID NO:3 of Walker et al. shares 97% homology with Applicants' SEQ ID NO:5. Secondly, nowhere does Walker et al. teach or suggest the claimed nucleic acid sequence which encodes a polypeptide having at least 60% homology to SEQ ID NO:2 and/or one or more Tome-1 activities. Although Walker et al. teaches SEQ ID NO:3, Walker et al. does ***not*** teach or suggest that SEQ ID NO:3 encodes CDC23, as asserted by the Office Action. Instead, Walker et al. teaches that SEQ ID NO:3 is ***coexpressed with*** the ***CDC23 gene***: "Column 1 is the SEQ ID number, column 2, the ***known cell cycle gene(s) with which the cDNA is most highly co-expressed***..." (page 8, lines 13-16, emphasis added). Walker et al. fails to teach or suggest that SEQ ID NO:3 encodes ***any polypeptide***, let alone a polypeptide having at least 60% sequence homology to SEQ ID NO:2 and/or one or more Tome-1 activities.

Even if SEQ ID NO:3 of Walker et al. were to encode a polypeptide, the Examiner has provided no evidence that this polypeptide would have at least 60% sequence homology to SEQ ID NO:2 and have one or more Tome-1 activities. First of all, the Examiner has provided no evidence that SEQ ID NO:3 is translated into a functional polypeptide. For instance, the cDNA may not contain a start codon, it may contain one or more missense mutations that cause it to be degraded, or it may contain a premature stop codon. Assuming arguendo that a polypeptide could be translated from SEQ ID NO:3 of Walker et al., the Examiner has provided no evidence that it would have one or more Tome-1 activities, as claimed by Applicants.

Thus, Walker et al. fails to teach or suggest all of Applicants' claim limitations. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejections of claims 1-3, 5-13 and 26 under §102(b) over Walker et al.

VII. CONCLUSION

Having addressed all outstanding issues, Applicants respectfully request reconsideration and allowance of the case. To the extent the Examiner believes that it would facilitate allowance of the case, the Examiner is requested to telephone the undersigned at the number below.

Respectfully submitted,

Dated: March 29, 2007

Judith L. Stone-Hulslander, Reg. No. 55,652
BANNER & WITCOFF, LTD.
28 State Street, 28th Floor
Boston, MA 02109
(617) 720-9600